

PATENT COOPERATION TREATY

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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT Rule 71.1)

Date of mailing
(day/month/year)

01.07.2004

Applicant's or agent's file reference
L2410-PCT

IMPORTANT NOTIFICATION

International application No.
PCT/BE 03/00109

International filing date (day/month/year)
24.06.2003

Priority date (day/month/year)
24.06.2002

Applicant
UNIVERSITE CATHOLIQUE DE LOUVAIN et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:



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INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

Applicant's or agent's file reference L2410-PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA/416)	
International application No. PCT/BE 03/00109	International filing date (day/month/year) 24.06.2003	Priority date (day/month/year) 24.06.2002
International Patent Classification (IPC) or both national classification and IPC G01N27/02		
Applicant UNIVERSITE CATHOLIQUE DE LOUVAIN et al.		

1.	This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2.	This REPORT consists of a total of 6 sheets, including this cover sheet.
	<input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
	These annexes consist of a total of 3 sheets.
3.	This report contains indications relating to the following items:
I	<input checked="" type="checkbox"/> Basis of the opinion
II	<input type="checkbox"/> Priority
III	<input type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	<input type="checkbox"/> Lack of unity of invention
V	<input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	<input type="checkbox"/> Certain documents cited
VII	<input type="checkbox"/> Certain defects in the international application
VIII	<input type="checkbox"/> Certain observations on the international application

Date of submission of the demand 06.11.2003	Date of completion of this report 01.07.2004
Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Joyce, D Telephone No. +31 70 340-3093



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/BE 03/00109**

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-22 as originally filed

Claims, Numbers

1-9, 11-27 as originally filed

10 filed with telefax on 09.06.2004

Drawings, Sheets

1/7-7/7 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

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5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-27
Inventive step (IS)	Yes: Claims	
	No: Claims	1-27
Industrial applicability (IA)	Yes: Claims	1-27
	No: Claims	

2. Citations and explanations

see separate sheet

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Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: WO 90/05300 (MIDWEST RESEARCH TECHNOLOGIES) 17 May 1990 (1990-05-17)
D2: US-A-5 922 537 (BOGLE GAVIN T ET AL) 13 July 1999 (1999-07-13)
D3: EP-A-0 402 917 (BIOCIRCUITS CORP.) 19 December 1990 (1990-12-19)
D4: WO 00/72018 A (ADVANCED ARRAY TECHNOLOGIES S ;HAMELS SANDRINE (BE); HOUBION YVES) 30 November 2000 (2000-11-30)
D5: WO 99/07879 A (FRAUNHOFER INST SILIZIUMTECHNO ;UNIV SOUTHERN CALIFORNIA (US)) 18 February 1999 (1999-02-18)
D6: WO 97/21094 A (INNOGENETICS NV ;IMEC INTER UNI MICRO ELECTR (BE); GERWEN PETER VA) 12 June 1997 (1997-06-12)
D7: US 2001/053522 A1 (ABE YOSHIHIKO ET AL) 20 December 2001 (2001-12-20)
D8: PATENT ABSTRACTS OF JAPAN vol. 011, no. 197 (P-589), 25 June 1987 (1987-06-25) & JP 62 019767 A (HITACHI LTD), 28 January 1987 (1987-01-28)
D9: WO 99/08105 A (CYRANO SCIENCES INC ;DIXSON JEFFREY (US); GRUBBS ROBERT H (US); LE) 18 February 1999 (1999-02-18)

(the documents D2 and D3 were not cited in the international search report).

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of independent claims 1 and 10 do not involve an inventive-step in the sense of Article 33(3) PCT.

The document D1 discloses (the references in parentheses applying to this document):

A method for capacitive detection of the presence of target sample on a substrate
(Page 2 line 4-8)

- binding a target sample to selective binding sites on the substrate (Page 3 line 1-10)
- target sample directly or indirectly labelled with conductive labels (Page 9 line 29-33)
- sensing the presence of the bound conductive labels to a binding site to determine the presence of the target sample (Page 9 line 37-Page 10 line 6)

The subject-matter of claim 1 therefore differs from this document in that:

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-sensing step is carried out by non-ohmic contacting, capacitive detection of the presence of the conductive labels.

The inventors problem may therefore be formulated as how to provide an alternative measurement technique for selective detection of binding events on a substrate.

Due to the fact that D1 gives a good hint that capacitive detection is possible concerning selective binding events within the summary of the background art (D1 Page 2 line 4-8) the skilled man would without a doubt have had knowledge of document D2 and incorporated its teaching.

Document D2 clearly shows (Col2 line 51-55) a bound moiety to a test surface wherein the first analyte is irreversibly affixed to the solid support and the second analyte is labelled with reporter particles selected from a wide range of functionalities (including conductive labelling, (cf D2 Col 9 line 16-19)) and can be used in neucleotide hybridisation assays (Col 3 line 17).

This document goes on to disclose that the label/tag is chosen so that a maximum capacitance change of each molecule is realised (D2 Col 14 line 22-25)

In light of these two documents it is considered that the subject-matter of presently worded claims 1 and 10 lack an inventive step in the sense of Article 33(3) PCT.

The additional feature which has been incorporated into newly filed independent claim 10 concerning the isolation of the electrode from the environment is merely one of several straight forward possibilities from which the skilled person would select, in accordance with circumstances, without the exercise of inventive skill, and is very well known in the art of sensor manufacture, see for example document D3 Col 13 line 46-51).

Dependent claims 2-9 and 11-27 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step.

Independent claims 1 and 10 are not in the two-part form in accordance with Rule 6.3(b) PCT, which in the present case would be appropriate, with those features known in combination from the prior art (document D1) being placed in the preamble (Rule 6.3(b)(i) PCT) and with the remaining features being included in the characterising part (Rule 6.3(b)(ii) PCT).

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CLAIMS

- 1.- A method for capacitive detection of the presence of target sample on a substrate, comprising the steps of:
 - binding a target sample to selective binding sites on the substrate, the target sample being directly or indirectly labelled with conductive labels,
 - sensing the presence of the bound conductive labels to a binding site to thereby determine the presence of the target sample,wherein the sensing step is carried out by a non-ohmic contacting, capacitive detection of the presence of the conductive labels.
- 2.- A method according to claim 1, furthermore comprising, before the binding step, a preliminary capacitance measuring step.
- 3.- A method according to claim 2, furthermore comprising a step of comparing the preliminary capacitance with the capacitance measured during the sensing step.
- 4.- A method according to any of the previous claims, wherein the labels are formed or enlarged prior to or during the sensing step.
- 5.- A method according to claim 4, wherein the labels are formed or enlarged by precipitation of a metal.
- 6.- A method according to any of the previous claims, wherein capacitance is measured as function of frequency to obtain a value representative of a electrical resistive property of the conductive label.
- 7.- A method according to any of the previous claims, wherein a global impedance is measured and the real part of the global impedance is used in addition to the capacitive part.
- 8.- A method according to any of the previous claims, furthermore comprising a step of optical detection of the presence of the label.
- 9.- A method according to any of the previous claims, furthermore comprising a step of magnetic or radioactive emissions detection of the presence of the label.
- 10.- Capacitive sensor device for determining the presence of a target sample in a solution, conductive labels being directly or indirectly couplable to the target sample, the capacitive sensor device comprising a substrate being able to selectively bind at a binding site or having attached thereto a binding site able to selectively bind a target sample, a capacitive sensor element, and sensing

circuitry for determining the presence of a target sample bound to the binding site by application of electrical signals to the capacitive sensor element, wherein the capacitive sensor element comprises a set of at least two electrodes with non-conductive surfaces in a region associated with the binding site which electrically isolate the electrodes from the solution used for the determination.

- 11.- Capacitive sensor device according to claim 10, wherein the intercapacitance value of the electrodes changes when detecting the presence of conductive labels at least when coupled to the target sample.
- 12.- Capacitive sensor device according to any of claims 10 or 11, wherein the set of electrodes are an array of parallel fingers which can be individually addressed in pairs.
- 13.- Capacitive sensor device according to any of claims 10 to 12, wherein the set of electrodes are interdigitated electrodes with parallel fingers, all fingers related to one electrode being short-circuited.
- 14.- Capacitive sensor device according to any of claims 10 or 11, wherein the set of electrodes are an array of crossed fingers whose intersections can be individually addressed in pairs.
- 15.- Capacitive sensor device according to any of claims 10 or 11, wherein the set of electrodes are a matrix of point electrodes.
- 16.- Capacitive sensor device according to any of claims 10 to 15, wherein a third electrode is provided insulated from the set of at least two electrodes, enabling the measurement of a second set of capacitive values.
- 17.- Capacitive sensor device according to any of claims 10 to 16, wherein the substrate comprises a semiconductive layer.
- 18.- Capacitive sensor device according to any of claims 10 to 17, wherein the presence of the conductive label creates a gate of a MOS or EEPROM like structure embedded in the semiconductor below the binding test sites.
- 19.- Capacitive sensor device according to any of claims 10 to 18, wherein the distance between the electrodes is reduced to a dimension comparable with the size of a single label.
- 20.- Capacitive sensor device according to claim 19, wherein the distance between two electrodes is 5 μm or less, preferably 2 μm or less.
- 21.- Capacitive sensor device according to any of claims 10 to 20, furthermore comprising a comparator unit, the outputs of the first and second capacitive

sensing elements or first and second groups of capacitive sensing elements being fed to a comparator unit.

- 22.- Capacitive sensor device according to any of claims 10 to 21, furthermore comprising an optical detector for determining the presence of the target sample.
- 5 23.- Capacitive sensor device according to any of claims 10 to 22, furthermore comprising a magnetic or radioactive emissions sensor for determining the presence of the target sample.
- 24.- Capacitive sensor according to any of claims 10 to 23, wherein the electrodes are made from a metal.
- 10 25.- Capacitive sensor according to claim 14, wherein the non-conductive surfaces are an oxide layer, a nitride layer, a paint or a lacquer.
- 26, - Capacitive sensor according to claim 24, wherein the metal is aluminium, and the non-conductive surfaces are formed by alumina.
- 15 27.- Capacitive sensor according to claim 24 or 25, wherein the metal is a non-noble metal.